

WHAT IS CLAIMED IS:

- 1 1. An antagonist of one or more of Rho family members characterized by the ability to elicit
2 neurite outgrowth from cultured neurons in an assay method, comprising the steps of:
3 (a) culturing neurons on a growth permissive substrate that incorporates a growth-
4 inhibiting amount of Rho family member; and
5 (b) exposing the cultured neurons of step a) to a candidate Rho family member
6 antagonist agent in an amount and for a period sufficient prospectively to permit
7 growth of the neurons;
8 thereby identifying as Rho family antagonists the candidates of step b) which elicit
9 neurite outgrowth from the cultured neurons of step a).
- 1 2. The antagonist according to claim 1, wherein said Rho family members are selected from
2 the group comprising RhoA, RhoB, RhoC, Rac, cdc42 and Rho-associated protein kinase.
- 1 3. The antagonist according to claim 1, wherein said interaction with the Rho regulatory
2 pathway is via interaction with GTP/GDP cycle.
- 1 4. The antagonist according to claim 3, wherein the interaction with the GTP/GDP cycle
2 involves GTP/GDP exchange proteins (GEP's); GDP dissociation inhibitors (GDI's); or
3 GTPase activating protein (GAP) to regulate Rho activity.
- 1 5. The use of antagonists of one or more Rho family members to promote neural growth by
2 inhibiting Rho family members in the central nervous system.
- 1 6. The use of ADP-ribosyl transferase C3, or other closely related toxins, to promote neural
2 growth by inhibiting one or more Rho family members in the central nervous system.
- 1 7. The use of a GTPase activating protein that is specific to Rho to convert GTP-bound
2 active Rho to GDP-bound inactive Rho.
- 1 8. The use of ADP-ribosyl transferase C3 according to claim 5, wherein said related toxins
2 are toxins A or B.

- 1 9. The use of biologically active fragments of ADP-ribosyl transferase C3, analogs and
2 derivatives thereof, to promote neural growth by inhibiting one or more Rho family
3 members in the central nervous system.
- 1 10. The use of Y27632, or related compounds, to promote neural growth by inhibiting Rho-
2 associated kinase in the central nervous system.
- 1 11. The use of genetically mutated forms of Rho, to promote neural growth by inhibiting one
2 or more Rho family members in the central nervous system.
- 1 12. The use of dominant negative Rho to inactivate Rho, to foster axon growth in the central
2 nervous system.
- 1 13. The genetically mutated form of Rho according to claim 11, wherein the mutation is in
2 the effector domain, A-37, thereby preventing GTP exchange.
- 1 14. The use of GDP dissociation inhibitors, or stimulation thereof, to inhibit the dissociation
2 of GDP from Rho and thereby prevent the binding of GTP necessary for the activation of
3 Rho.
- 1 15. A method for producing Rho antagonists from Rho family members, fragments, analogs
2 of derivatives by peptide synthesis or by recombinant DNA expression of either a
3 truncated domain of Rho family members, incorporating one or more L- or D-amino acid
4 substitutions, or of intact Rho family members using standard recombinant procedures
5 and selecting antagonist characterized by the ability to elicit neurite outgrowth from
6 cultured neurons in an assay method, comprising the steps of:
7 (a) culturing neurons on a growth permissive substrate that incorporates a growth-
8 inhibiting amount of a Rho family member; and
9 (b) exposing the cultured neurons of step a) to a candidate Rho family member
10 antagonist agent in an amount and for a period sufficient prospectively to permit
11 growth of the neurons;
12 thereby identifying as Rho family antagonists the candidates of step b) which elicit
13 neurite outgrowth from the cultured neurons of step a).

1 16. The antagonist according to claim 1, wherein derivatives of Rho family members, Rho
2 family members fragments and Rho family members analogs can be generated by
3 chemical reaction of the parent substance to incorporate the desired derivitizing group,
4 such as N-terminal, C-terminal and intra-residue modifying groups that have the effect of
5 masking or stabilizing the substance or target amino acids within it.

1 17. An antagonist of one or more of Rho family members, characterized by the following
2 properties:

- 3 (a) blocks growth inhibition of neurites by myelin or myelin proteins; and
4 (b) interferes with Rho family members-mediated growth inhibition as competitive but
5 non-functional mimics of endogenous Rho family members.

1 18. A composition comprising a therapeutically effective amount of the composition of claim
2 1 in a suitable pharmacologic carrier.

1 19. An assay method useful to identify Rho family member antagonist agents that suppress
2 inhibition of neuron growth, comprising the steps of:

- 3 (a) culturing neurons on a growth permissive substrate that incorporates a growth-
4 inhibiting amount of a Rho family member; and
5 (b) exposing the cultured neurons of step a) to a candidate Rho family member
6 antagonist agent in an amount and for a period sufficient prospectively to permit
7 growth of the neurons;
8 thereby identifying as Rho family antagonists the candidates of step b) which elicit
9 neurite outgrowth from the cultured neurons of step a).

1 20. A kit to test for Rho family antagonists that can be used to promote neurite growth
2 comprising the components necessary to work the method of claim 16, in a suitable
3 container.

1 21. A method to suppress the inhibition of neuron, comprising the steps of delivering, to the
2 nerve growth environment, a Rho family antagonist in an amount effective to reserve
3 myelin inhibition.